

0.1N hydrochloric acid to give a stock solution of convenient concentration containing not less than 150 micrograms of demeclocycline hydrochloride per milliliter (estimated). Blend for 3 to 5 minutes. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.100 microgram of demeclocycline hydrochloride per milliliter (estimated).

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11162, Mar. 17, 1978; 50 FR 19920, May 13, 1985]

§ 446.120 Doxycycline hyclate oral dosage forms.

§ 446.120a Doxycycline hyclate capsules.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Doxycycline hyclate capsules are composed of doxycycline hyclate and one or more suitable and harmless lubricants and diluents enclosed in a gelatin capsule. Each capsule contains doxycycline hyclate equivalent to either 50, 100, or 300 milligrams of doxycycline. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of doxycycline that it is represented to contain. The moisture content is not more than 5.0 percent. It passes the identity test for the presence of the doxycycline moiety. The doxycycline hyclate used conforms to the standards prescribed by § 446.20.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The doxycycline hyclate used in making the batch for potency, moisture, pH, doxycycline content, identity, and crystallinity.

(b) The batch for potency, moisture, and identity.

(ii) Samples required:

(a) The doxycycline hyclate used in making the batch: 10 packages, each

containing approximately 300 milligrams.

(b) The batch: A minimum of 36 capsules.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Blend a representative number of capsules in a high-speed glass blender jar containing 0.1N hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of doxycycline per milliliter (estimated). Blend for 3 to 5 minutes. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.100 microgram of doxycycline per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *Identity.* Proceed as directed in § 436.308 of this chapter, except prepare the standard and sample solutions as follows: Dissolve precise amounts of the doxycycline capsule contents and of the doxycycline working standard in methanol and further dilute each solution to a concentration of 1 milligram of doxycycline per milliliter. Prepare the sample-standard mixed solution by mixing equal volumes of the final standard and sample solutions. The standard and sample must each produce a major, yellow fluorescent spot with the same R_f value, and the standard-sample mixed solution must show no separation of major spots.

[39 FR 19076, May 30, 1974. Redesignated at 39 FR 41250, Nov. 26, 1974, and amended at 43 FR 11162, Mar. 17, 1978; 44 FR 20667, Apr. 6, 1979; 50 FR 19920, May 13, 1985]

§ 446.120b Doxycycline calcium oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Doxycycline calcium oral suspension is prepared from doxycycline hyclate and contains one or more suitable and harmless buffer substances, preservatives, diluents, solvents, colorings, and flavorings. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of doxycycline that it is represented to contain. Its pH is not less than 6.5 and

not more than 8.0. It passes the identity test for the presence of the doxycycline moiety. The doxycycline hyclate used conforms to the standards prescribed by § 446.20(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The doxycycline hyclate used in making the batch for potency, moisture, pH, doxycycline content, identity, and crystallinity.

(b) The batch for potency, pH, and identity.

(ii) Samples required:

(a) The doxycycline hyclate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 6 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Transfer an appropriate aliquot of the suspension to a volumetric flask and dissolve with sufficient 0.1N hydrochloric acid to give a stock solution of convenient concentration (containing not less than 150 micrograms of doxycycline per milliliter in acid). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.100 microgram of doxycycline per milliliter (estimated).

(2) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted sample.

(3) *Identity.* Proceed as directed in § 436.308 of this chapter, except prepare the standard and sample solutions as follows: Dissolve precise amounts of the doxycycline calcium oral suspension and of the doxycycline working standard in methanol and further dilute each solution with methanol to a concentration of 1 milligram of doxycycline per milliliter. Prepare the sample-standard mixed solution by mixing equal volumes of the final concentration of the sample and standard solutions. The sample and standard must each produce a major, yellow flu-

orescent spot with the same R_f value, and the sample-standard mixed solution must show no separation of major spots.

[39 FR 41250, Nov. 11, 1974, as amended at 45 FR 16476, Mar. 14, 1980; 50 FR 19920, May 13, 1985]

§ 446.120c Doxycycline hyclate tablets.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Doxycycline hyclate tablets contain doxycycline hyclate with or without one or more disintegrants, lubricants, colorings, and coating substances. Each tablet contains doxycycline hyclate equivalent to 50 or 100 milligrams of doxycycline. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of doxycycline that it is represented to contain. Its moisture content is not more than 5.0 percent. It passes the dissolution test. It passes the identity test. The doxycycline hyclate conforms to the standards prescribed by § 446.20(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The doxycycline hyclate used in making the batch for potency, moisture, pH, doxycycline content, identity, and crystallinity.

(b) The batch for potency, moisture, dissolution, and identity.

(ii) Samples required:

(a) The doxycycline hyclate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 100 tablets.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place a representative number of tablets into a high-speed glass blender jar containing 0.1N hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of doxycycline per milliliter (estimated).